Medical Device Labeling -- Suggested Format and Content

Draft Document

This guidance document is being distributed for comment purposes only.

Office of Device Evaluation

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[Note: This DRAFT document represents the agency's attempt to obtain public comment on the labeling of medical devices. Comments and suggestions may be submitted at any time until the close of the comment period as specified in a notice of availability which will be published in the Federal Register in the near future. The comment period will be at least 90 days. Submit comments for agency consideration by writing to Dan Spyker, CDRH, 9200 Corporate Boulevard, HFZ-450, Rockville, MD 20850 or by e-mail to dxs@cdrh.fda.gov. For questions regarding the use or interpretation of this guidance, also contact Dan Spyker at (301) 443-8320.

This guidance was initially placed on the FDA home page with an incorrect cover sheet on April 21, 1997. This version corrects those errors and supersedes that version.]

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Center for Devices and Radiological Health

INTRODUCTORY NOTES

Labeling requirements for medical devices have been established in the Food, Drug, and Cosmetic Act (the act), 21 U.S.C. Title 21 and in the regulations promulgated under the act in the Code of Federal Regulations. For example, general labeling requirements can be found in 21 CFR Part 801 while detailed and specific labeling requirements for in vitro diagnostic products appear at 21 CFR 809.10. Neither the act nor the regulations, however, provide specific definitions or explanations of some significant labeling terms such as warnings, precautions, contraindications and adverse events. Because labeling is a key factor in the FDA clearance of 510(k)s and approval of PMAs, it is important that ODE reviewers have a common understanding of how these terms and other elements of labeling are designed and evaluated in order to have consistent and uniform premarketing evaluation of device labeling. It is also important for device manufacturers to understand FDA's approach to labeling evaluation.

In an effort to promote uniformity and clarity in labeling reviews, ODE issued a Blue Book Memorandum #G91-1 on March 8, 1991, entitled, "Device Labeling Guidance". This guidance has been in use since it was issued but CDRH studies and experience have demonstrated a need for greater direction in the format and content of device labeling. Therefore, this updated and expanded guidance has been drafted for comment. When finalized, it will supersede and replace G91-1.

The attached draft guidance identifies a suggested content for device labeling and each element of the suggested labeling is discussed. The guidance also includes a description of essential prescribing information for medical device labeling. As with all agency guidance documents, this guidance will not be mandatory; it will only provide guidance to assist in the preparation and review of labeling. Furthermore, this guidance will not be retrospective; it is intended for use in labeling that is prepared subsequent to the issuance of a final document.

In addition to this guidance on device labeling, FDA is considering the development of a new device labeling regulation. If a new device labeling regulation is promulgated, this guidance will be superseded and replaced, as circumstances dictate. Comments received on this draft guidance will be considered in the preparation of a final guidance document and in the preparation of a proposed labeling regulation.

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Table of Contents

Numbers in square brackets [ ] refer to citations in the Guidance for this Bibliography

Overview

This table of contents for the *Information for Prescribers* suggests the structure (order of the labeling sections). The balance of the document outlines the content of each section of the device labeling. This guidance:

- is intended to apply to devices approved *via* premarket approval (PMA) and those cleared *via* premarket notification (510(k)) applications
- is intended to apply to both prescription and non prescription (over the counter, OTC) medical devices
- should be applied as appropriate to suit the device (one size doesn't fit all), see individualization of labeling format and Table 1.
- is NOT intended to apply to labeling for *in vitro* diagnostic products which are already covered by regulation (21 CFR 809.10)
- is NOT intended to supplant existing regulations (21 CFR 801) or device-specific labeling guidance (801.403) that has been developed in conjunction with industry through appropriate rule making procedures.
- is NOT a change of policy, but a clarification and extension of current guidance including Blue Book Memorandum, #G-91-1, *Device Labeling Guidance*, March 8, 1991 [1]

Individualization of Product Labeling

All product packages (except surgical instruments) must bear a label (display of written, printed or graphic matter upon the immediate container of any article or on the article itself) including the name of the device, the manufacturer, and the address of the manufacturer. This

Labeling refers to all labels and other written, printed or graphic matter: 1) upon any article or any of its containers or wrappers, or 2) accompanying such articles (Section 201(m) of the Federal Food, Drug, and Cosmetic Act) [2]. This definition is generally extended to include audio or video recordings whether in analog or digital format.

It is critical that you write labeling so that the intended target audience can read and understand it. We refer you to "Write It Right: Recommendations for Developing User Instruction Manuals for Medical Devices Used in Home Health Care [ref 10] for general principles to assist you in preparing effective labeling.

Inclusion in the labeling of a disclaimer regarding the safety and effectiveness of the device for its indicated or intended use is to be avoided. Instead, labeling should include an objective and accurate representation of the clinical experience with the device whereby the practitioner and patient are made aware not to expect a completely safe and effective outcome with the use of the device in all cases. All sections of the labeling, particularly INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE EVENTS, and CLINICAL STUDIES, should reflect this balance.

The detail of the product labeling should be appropriate for the needs of the user of the device as summarized in Table 1.

Table 1. Sections to be included in Device Labeling

Section of Information for Prescribers	Device directions for use known to an ordinary individual	Device with Minimal Labeling	Clinical Data not the Basis of Device Marketing	Clinical Data Supporting Device Marketing
Essential Prescribing Information	-	as needed	yes	yes
1. BRIEF DEVICE DESCRIPTION	Name	yes	yes	yes
2. INTENDED USE / INDICATIONS	-	yes	yes	yes
3. CONTRAINDICATIONS	-	if any	yes	yes
4. WARNINGS	-	-	yes	yes
5. PRECAUTIONS	-	-	yes	yes
6. ADVERSE EVENTS	-	-	as available	yes
7. CLINICAL STUDIES	-	-	-	yes
8. INDIVIDUALIZATION OF TREATMENT	-	-	as needed	yes
9. PATIENT COUNSELING INFORMATION	-	as needed	as needed	as needed
10. CONFORMANCE TO STANDARDS	-	if any	yes	yes
11. HOW SUPPLIED	-	as needed	as needed	as needed
12. OPERATOR'S MANUAL	-		as needed	as needed
13. PATIENT'S MANUAL	-	-	as needed	as needed
14. REFERENCES	-	-	as needed	as needed

Medical devices having commonly known directions (801.116) is one for which "adequate directions for common uses are known to the ordinary individual" and it is for that reason exempt from 502(f)(1) (adequate directions for use). Examples include band-aids (non-medicated) and tongue depressors.

Under certain circumstances, the immediate container may be of a size that would not support all the information expected on the label. Examples of devices fitting this description include: over-the-counter (OTC) contact lens lubricating and rewetting drops (small bottle sizes). In such cases, it is appropriate for the immediate package to be minimally labeled and should also include a statement that refers the user to additional labeling that will accompany the product (e.g., package insert) for details regarding contraindications, warnings, precautions, etc.

For a **Device with Minimal Labeling**, the labeling should include a description (including the generally recognized name and manufacturers name and model ID), a statement of the indications and other information as needed.

For a device where **Clinical Data are Not the Basis of Device Marketing**, Section 7 may not be necessary. Each of the other sections may be included in the labeling or not as appropriate to reflect the safety and performance characteristics of the medical device.

For most medical devices approved via PMA, there is **Clinical Data Supporting Device Marketing**. The labeling for most PMA approved devices will include all 14 sections.

Prescription devices are are exempt from adequate directions for use for the lay person under certain conditions (see 21 CFR 801.109).

Information for Prescribers

The Essential Prescribing Information (EPI) and the sections numbered 1-14 comprise the Information for Prescribers. The complete medical device labeling includes this (Information for Prescribers) along with the complete Operator's Manual, Patient's Manual, the package labels, and promotional material.

For complex medical devices, a separate Operator's Manual and Patient's Manual may be appropriate. For such devices, the sponsor may wish to include a brief description and/or a table of contents in the Information for Prescribers.

ESSENTIAL PRESCRIBING INFORMATION (EPI)

The CDRH believes manufacturers would communicate more effectively with practitioners and users of medical devices if the most important labeling information were organized into a brief structured abstract of key prescribing information. The EPI is intended to provide an overview and a refresher for those already familiar with the full labeling. The EPI provides cross reference to the full labeling. The EPI should be non-promotional, consistent with the full labeling, is expected to be not more than one page in length, and should utilize icons and illustrations to maximize utility to the user. A suggested format is included at the end of this guidance.

The EPI represents an agency-wide effort including the Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, and CDRH, to provide highlights of prescribing information in a consistent format.

EPI -- Suggested Format

Manufacturer's Name, Device Name and Model

Date of this labeling (or revision)

Essential Prescribing Information

Numbers in parentheses ( )refer to sections in the main part of the product labeling

Device Description

Brief description of what the device is and what it is intended to do.

Boxed WARNING (if needed)

Critical information, particularly problems that might result in death or serious injury that should be considered when prescribing the device.

New Information

Significant information that is appended, changed or deleted, within 6 months of the labeling change. After 6 months, the information is no longer presented here.

Intended Use/Indications

Specific therapeutic or diagnostic use(s). Approved *clinical* "Indications" indicated in the premarket submission(s) (PMAs or 510(k)s). Clinical testing and data should exist to support these claims. (2)

Individualization of Treatment

Information to assist the clinician in determining if this device is appropriate for this patient. Includes:

- Limitations on its use (physical, not clinical),
- Set-up recommendations and precautions,
- Administering guidelines (preferably professional society) and their application to this device, and
- Features or functions for specific populations. (8.1)

Contraindications

Clinical situations where this specific device should NOT be used. (3)

Warnings and Precautions

Information that must be followed for safe use. This should NOT be a an exhaustive list of warnings, but limited to those that have severe consequences and are specific to this device. (4,5)

Adverse Events

Undesirable effect reasonably associated with the use of this device. Serious events which occur with such frequency that the clinician needs to be warned. (6)

Maintaining Device Effectiveness

Conditions (e.g., use duration, component replacement) that must be managed during normal use to maintain the safety and effectiveness of the device. (12.1)

Use in Specific Populations

Use in populations with special needs such as pregnant women, neonates and the elderly. If the device is appropriate for these populations, the changes or modifications that must be made and the precautions that must be followed for safe use. (8.1)

Patient Counseling Information

What the patient should know. This includes information for the clinician to counsel patients, and if necessary, guidelines on informed consent. (9)

How Supplied

How the basic device is supplied and what additional equipment is required for safe use. This is not a list of all options, but rather a simple list to assure that all necessary components are considered for safe use. (11)

Prescription Legend

A prescription device, as defined under 21 CFR 801.109 is considered unsafe except under the supervision of a practitioner licensed by law to direct the use of the device (21 CFR 801.5). A prescription device is misbranded if its package label does not bear the following statement:

Caution: Federal Law restricts this device to sale by or on the order of a physician (or properly licensed practitioner).

The prescription legend should also appear prominently at the beginning or the end of device labeling.

The first three sections of the labeling, DEVICE DESCRIPTION, INDICATIONS and CONTRAINDICATIONS, should appear on the same page, ideally the first page, of the product labeling.

1. BRIEF DEVICE DESCRIPTION

Under this section heading, the labeling should include a brief description of the device, how the device functions, the ingredients where appropriate, and its significant physical and performance characteristics. The description should contain the information most likely to be useful to the practitioner/user. Graphic illustrations may be used to supplement the text as appropriate. The balance of the description should be contained in *Detailed Device Description* (section 12.2).

Promotional prose should be scrupulously avoided in these sections. Quantitative description is generally more useful than qualitative comments. Description of the function of the device (as compared to outcome) is appropriate for the description section.

2. INTENDED USE / INDICATIONS

This section should succinctly state what the device does (Intended use) and in what patient population (Indications).

"Intended Use" refers to the functional capability of the device. It also refers to the objective intent of the persons legally responsible for the labeling of the device. The intent is determined by their expressions or may be shown by the circumstances surrounding the distribution of the device. This objective intent may be shown by labeling claims, advertising matter, or oral or written statements by such representatives. It may be shown by the offering or the using of the device, with the knowledge of such persons or their representatives, for a purpose for which it is neither labeled nor advertised (21 CFR 801.4).

"Indications" are the disease(s) or condition(s) the device will diagnose, treat, prevent, cure, or mitigate and a description of the target population for which the device is intended without causing unreasonable risk of illness or injury associated with the use of the device.

Indications should be supported by valid scientific evidence that the device as labeled will provide clinically significant results. Scientific evidence of effectiveness per 21 CFR 860.7

should be based on well-controlled investigations, partially controlled studies, studies without matched controls, well-documented case histories, or reports of significant human experience. Evidence may vary depending upon the device, conditions of use, existence and adequacy of warnings, and extent of experience with the device.

As appropriate, the labeling should state that the device (trade name) is "indicated for use":

- in the treatment, mitigation, prevention, diagnosis or monitoring of a recognized disease or condition or an important manifestation of a disease or condition; and/or
- in the relief or mitigation of symptoms associated with a disease or condition; and/or
- as an aid or adjunct to a mode of therapy or diagnosis.

The indications labeling may also include:

- the part of the body or type of tissue applied to or interacted with;
- frequency of use;
- physiological purpose; or
- important limitations, e.g., for use in operating room only.

3. CONTRAINDICATIONS

Contraindications are conditions under which the device should not be used because the risk of use clearly outweighs any possible benefit.

Known hazards (not theoretical possibilities) are to be listed, e.g., if hypersensitivity to a material in the device has not been demonstrated, it should not be a contraindication.

Contraindications to the use of a device could include:

- Demonstrated hypersensitivity to a material of a patient-contacting device
- Substantial risk of being harmed because of patient characteristics (age, gender, concomitant therapy, disease state, *et al*); or
- Continued use in the face of an unacceptably hazardous adverse event.

If no contraindications are known, this section of the labeling should state "None known".

Both the Warnings and Precautions sections of your labeling provide information on how to avoid hazards, i.e., sources of harm. Here we provide guidance on what information should be in each of these sections and how to present that information most clearly and succinctly.

We still recommend that you write a separate **Warnings** section and **Precautions** section in your labeling.

4. WARNINGS

Boxed WARNING

Special problems, particularly those that may lead to death or serious injury, may be required by FDA to be placed in a prominently displayed box. The boxed warning ordinarily is based on clinical data, but compelling animal data may also be the basis of a boxed warning. Most labels will not require a boxed warning. If a boxed warning is required, it should be located where it is easily seen, e.g., at the beginning of the labeling or immediately following the brief DEVICE DESCRIPTION.

Definitions

Warnings and **Precautions** tell readers about hazards other than those that are contraindications to device use. There are many words in broad use to present hazards (e.g. danger, alert, hazard, attention). Medical product labeling has traditionally used the words "warnings" and "precautions". They are the terms that appear in the labeling regulations and are familiar to clinical users of devices.

The difference between the two is a matter of degree of the likelihood and seriousness of the hazard for this device. It also depends, in part, on: the indications for use, the target population, whether the device is an implant, the potential for improper care or misuse of the device, whether the device is for over-the-counter or prescription use, and whether it is subject to existing device-specific guidance or predicate device labeling.

Adverse events listed in the WARNINGS or PRECAUTIONS sections are still subject to the reporting requirements of the Medical Device Reporting (MDR) regulation (21 CFR 803).

Warnings alert the user to potential serious outcomes (death, injury, or serious adverse events) to the patient or user.

Examples of warnings:

Warning: Do not expose patient to MRI. Strong magnetic fields may affect the device, causing injury to the patient.

Warning: Always insert (name of device) before sex. Leave it in for at least 6 hours. If you do not do this, you may become pregnant.

5. PRECAUTIONS

Precautions alert the reader to exercise special care necessary for the safe and effective use of the device. They may include actions to be taken to avoid effects on patients or users that may not be potentially life threatening or result in serious injury, but about which the user should be aware. Precautions may also alert the user to adverse effects on the **device** of use or misuse and the care necessary to avoid such effects.

The Precautions section should not contain statements that: (1) belong in other sections of the labeling, e.g., warnings or maintenance information, or (2) do not reflect the immediacy and level of importance of a hazard alert.

Examples of precautions:

Caution: Do not resterilize. Contents may be damaged or distorted.

Caution: Do not fire the autoinjector without a syringe in place, as this may damage the plunger and cause it to fail..

Caution: Do not expose the device to temperatures below x_°C (y_°F), as such exposure may cause the device's memory to fail.

Caution: Inspect sealed sterile package before opening. If seal is broken, contents may not be sterile and may cause infection in the patient.

Note: The signal word commonly used for a single precaution is CAUTION. See discussion of signal words.

Content and Format

The way in which a warning or precaution presents information is critical to the reader's ability to notice, understand and respond to it. Many researchers have examined how to effectively present such information (see, for example, references 3-9). We base our recommendations for the content and formatting of warnings and precautions in medical device labeling on this research. The purpose of each of these two sections is to present a particular type of hazard information. Although the type(s) of hazards described in each of the sections will be different, the way you should present information will be very similar. Your objective is to get the reader's attention, inform him or her of the level of seriousness of the hazard and recommend steps to avoid the hazard.

Content Elements

There are four generally recognized elements in an effective hazard alert:

- **a signal word** (WARNING, CAUTION) to alert the reader that what follows is important hazard information. The signal word commonly used for a single precaution is CAUTION. A symbol or icon may emphasize the effect of the signal word. Additional enhancement, such as bolding, larger type, underlining, italics, or color may help the information stand out from the rest of the text.

- a **hazard avoidance directive** in the form: **Do Not, Never, Avoid...”** (or **Do**, if more appropriate) followed by the action to avoid (or perform). The objective of this directive is to give clear instructions to the user on how to avoid the hazard. In a precaution, the hazard avoidance directive is the special care instruction (e.g., protection of the device from a particular environmental condition).

- an **identification of the hazard** associated with the warning (e.g., allergic reaction to material, strong magnetic field) or precaution (e.g., environmental effect, damage from resterilization).

- the **consequences**, specifying the serious adverse events, potential safety hazards and limitations in device use that result if users do not follow instructions, to give them a clear idea of the risk. Hazard alert research has shown that this element has a significant effect on readers. If it is not included, the alert is likely to be less effective.

The signal word should appear first. For a list of warnings or precautions, one signal word at the head of the list may be sufficient. For a list of precautions, the header PRECAUTIONS would be appropriate. The order provided here for the other three elements (hazard avoidance, hazard identification, and consequences) will be appropriate for most instances, but may be altered as necessary to best communicate the information to the reader.

In some instances, including an alternative action to that which you are warning against may increase the user’s motivation and ability to comply with the warning. If the description of the alternative is brief, it might be included as part of the hazard avoidance directive. If the description or direction requires more than a sentence, include it as a procedural step following the warning or precaution to avoid diluting the effect of the warning or precaution.

Examples of included alternative action:

Warning: Do not use latex catheter to drain CSF from the third ventricle. Such use may increase the potential for inflammatory cerebritis. Use a commercially available shunt intended for this procedure.

Warning: Always use the recommended neutralizer with your disinfecting solution to neutralize the lenses before applying them to your eyes. Disinfecting solution contact with eyes may cause burning, stinging or redness.

General Writing Recommendations

Hazard alert information (warnings, precautions) should be as concise as possible while providing complete information. We recommend using bullets, rather than full sentences. Each bullet should contain a single item. Grouping warnings or precautions in paragraph form is not recommended. Use white space to enhance the visibility of each individual item.

A warning or precaution that applies **only** to a **specific** instruction or action should precede the instruction to which it applies. Readers are not likely to understand such hazard alerts if they are included in lists of general warnings and precautions. Worse yet, users may not remember a warning or precaution when reading the instructions if the hazard information is not adjacent to the instruction.

Example of a hazard alert that should proceed a specific instruction:

CAUTION! Open stopcock just before engaging xxx to avoid over expansion of yyy.

If it makes sense, such warnings and precautions may appear in both places.

Example of an alert that might appear in both a general list of warnings and just before a specific procedural step:

Hand washing is necessary before several steps in device use to prevent infection. *(One bullet in a list of warnings)*

WARNING! Wash hands thoroughly before next step. Failure to do so may lead to infection. *(Warning placed just before the specific instruction)*

Specifics for Each Section

Warnings

When there is a hazard that may lead to an adverse outcome for a person based on reasonable evidence of its association with the use of the device, include a **warning** on this hazard. A causal relationship need not have been proven. A warning may be appropriate when the device is commonly used for a disease or condition for which there is a lack of valid scientific evidence of effectiveness for that disease or condition and such usage is associated with a serious risk or hazard.

Precautions

When there is a hazard that may lead to device malfunction, device failure, damage to the device, or damage to other property, include, as a **precaution**, the information the user needs to avoid the hazard. A precaution may be needed if misuse may cause the device to function inappropriately rather than actually fail.

If device malfunction, failure or damage resulting from misuse may seriously harm the patient or user, list this hazard information as a WARNING.

When the WARNINGS or PRECAUTIONS section contains a large number of items, a hierarchical structure (organizing the warnings into subsections, perhaps with bullets) can improve the readability. When the number is large due to collection warnings or precautions from the OPERATOR'S MANUAL, consideration should be given to eliminating some of the less important precautions to avoid "dilution" (detracting from the value and readability due to large numbers).

6. ADVERSE EVENTS

An adverse event (AE) is an undesirable effect, associated with the use of the device. This section is not a repeat of the Contraindications, Warnings and Precautions sections. It is, rather, a list of the adverse events seen in clinical studies with the associated frequency data.

Any potentially fatal adverse events should be included in the "Warnings" section or, if appropriate, the "Contraindications" section of the labeling as appropriate.

Frequency data should be based on adequately reported clinical studies. The adverse events section should include four parts presented in the following order:

a) a clear description of the safety sample (number of patients, number of devices), total device exposure (patient years), and mean and range of individual patient exposure;

b) a statement of total patient deaths and an appropriate description of any device-related deaths;

c) as available, a tabulation of the observed AEs, including those considered minor or readily resolved. AEs should be listed in descending order according to frequency or in some other logical order. The basis of the ordering should be explicitly stated; and

d) a list (optionally with a brief discussion) of AEs which might be expected (potential AEs), but have not been observed in the clinical studies. AEs should be listed alphabetically or in some other logical order. The basis of the ordering should be explicitly stated.

The listing of the AEs should be followed, if appropriate, by statements directing the reader to other sections of the labeling for additional information regarding these adverse eventss and any steps that should be taken.

For a device approved under Premarket Notification (510(k)) which was not supported by clinical studies, the detail in AE section would reflect the available data.

MDR Reporting Reminder: Medical device manufacturers and users are required by law and regulation to report serious injuries and death.

7. CLINICAL STUDIES

This section would not be included in labeling of a device approved under Premarket Notification (510(k)) which was not supported by clinical studies.

Information in this section should include a brief summary -- a self-contained description of the design, conduct, and most important results of the clinical studies conducted in support of this labeling. It should describe the:

a) A brief introductory section including

- the **purpose of the studies**: be specific, the purpose is to support the indicated use, not to show that the device is "safe and effective"; and

- the **study design**: e.g., "A multicenter, double-blind comparison of"... One or two sentences should suffice;
- primary endpoints

b) **Patients studied**: number of patients in each group, gender, ethnic origin, disease category, age range, principal and unusual inclusion and exclusion criteria;

c) **Methods**: a concise statement of the methodology involved in gathering the primary effectiveness and safety data; and

d) **Results**: effectiveness and safety, usually summarized in a table: *Principal Effectiveness and Safety Results*. Avoid promotional prose. Avoid use of the words "safe" and "effective" in the description of the study and results, except as suggested for the table title.

In the situation where no clinical study was conducted (e.g., a PMA supplement without a labeling change), the evidence which supported the efficacy claims for the original PMA, or whatever evidence is the most pertinent, should be presented.

8. INDIVIDUALIZATION OF TREATMENT

This section might not be included in labeling of a device approved under Premarket Notification (510(k)) where such information is not appropriate.

Information under this section is intended to assist the practitioner in determining whether the device is appropriate in the treatment, mitigation, prevention or diagnosis of a recognized disease or condition or important manifestation of a disease or condition **in a particular patient.** This section should contain data on the limitations of device performance, administration guidelines, and the use of the device in the target population for which it is intended.

This information should be derived from the clinical studies (see section 7) or other sources of valid scientific evidence and address the following if known:

- specific conditions that should be met before the device is used on a long-term basis, e.g., demonstration of responsiveness to the device in a short term trial or whether the indications for long-term use are different from those for short term use;
- specific tests needed for the selection or monitoring of the patients;
- information on the type of improvement expected from use of the device and the anticipated degree and duration of improvement; and
- information on the recommended intervals between device use, duration of treatment, or any modifications of such.

When there is a common belief that the device may be effective for a certain use or there is a common use of the device for a condition but the preponderance of evidence related to the use or condition demonstrates that the device is ineffective, FDA may require that the labeling state that there is a lack of evidence that the device is effective for that use or condition.

8.1 Use in Specific Populations

If information on the use of a device in a specific population meets the criteria for a contraindication, warning, or precaution, include that information in the appropriate section. Refer the reader to that section, e.g., "See WARNINGS section for more information on..." Some specific population information may be most appropriately presented in the INDICATIONS section.

Pregnancy, Labor and Delivery -- If the device has the potential for direct or indirect harm to the fetus, describe available reproductive studies in both animals and humans; if used during labor or delivery, describe available information about its effect on the mother and fetus.

Nursing Mothers -- This would apply if a device component was absorbed systematically and could potentially be excreted in human milk.

9. PATIENT COUNSELING INFORMATION

The information in this section reminds the physician of points to consider in counseling the patient about the device. The manufacturer is most knowledgeable about the unique characteristics of the device that may be important to inform the patient. It should be remembered that patient counseling may be delegated to someone other than a knowledgeable physician, such as a nurse or distributor representative.

10. CONFORMANCE TO STANDARDS

The device labeling may contain reference, by standard number and title, and date to adopted applicable medical device, materials, or process standards or specifications used in its manufacture or evaluation.

11. HOW SUPPLIED

Describe how the basic device is supplied and what additional equipment is required for safe use. It should also reference relevant factors such as: fully assembled or non-assembled, sterile or non-sterile, disposable or non-disposable, number in each package (10, 25, and 50 per package), or quantity in each packages (4 oz, 8 oz, and 12 oz sizes), etc.

This is not a list of all options, but rather a simple list to assure that all components necessary for use are considered.

12. OPERATOR'S MANUAL -- Brief Description

For complex medical devices, especially those which are programmable (software controlled), the Operator's Manual (user manual, reference manual) is typically quite long. This section of the Information for Prescribers may contain all of the OPERATOR'S MANUAL or a brief description and/or the table of contents of the OPERATOR'S MANUAL.

Where the OPERATOR'S MANUAL is a separate document, it should include the Information for Prescribers, especially the INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS. Many manufacturers comply with this recommendation by attaching a copy of the Information for Prescribers at the beginning or end of the OPERATOR'S MANUAL.

12.1 Maintaining Device Effectiveness

Describe conditions, e.g., use duration, component replacement, that should be managed during normal use to maintain the safety and effectiveness of the device.

12.2 Complete Device Description

This section should contain the complete device description (summarized in Section 1. BRIEF DEVICE DESCRIPTION). The description includes information on the materials and/or ingredients to which users or patients will be exposed.

12.3 Directions for Use

The term "Directions for Use" means directions under which the practitioner or lay person can use a device safely and for its intended purpose(s). For a prescription device this section may include some of the salient points for device use and refer the reader to the OPERATOR'S MANUAL.

Take care to write labeling so that the intended target audience can read and understand it [10].

For devices designed for home use, "Directions for Use" means directions under which the lay person can use a device safely and for the purposes for which it is intended. The labeling should include information on:

- the frequency of use of the device;
- the time of use;
- signs/symptoms, indications, adverse events;
- the route and method of use; and
- the preparation for use of the device.

and other information as appropriate.

13. PATIENT'S MANUAL -- Brief Description

Information for the patient is frequently packaged in a separate booklet with appropriate prose and illustrations. This section of the Information for Prescribers may contain all of the PATIENT'S MANUAL or a brief description and/or the table of contents of the PATIENT'S MANUAL.

Information for the patient is labeling prepared by a manufacturer and intended to be given to patients (or family members or other lay persons caring for patients) to inform them about a device or procedure using a device. Such labeling may, as necessary, assist in deciding on a type

of device, a procedure or treatment using a device, select from an array of similar devices, and instruct on how to use (e.g., set up, operate, clean, interpret the results of, maintain, and store) the device. This labeling is distinguished from Patient Counseling Information in that it is prepared for direct use by patients and lay persons.

This labeling may include information sheets, booklets, and other audio-visual materials designed to assist the patient in decision making about the use of the device, or user instructions specifically intended for the lay user [10, 11]. Appropriate professional organizations may provide useful materials that can contribute to the development of patient information labeling by giving information and terminology.

In determining whether patient information labeling is appropriate for a device, consider the needs of the patient, such as:

- What information about the device, such as risks and benefits, alternative treatments, or effect on lifestyle, does the patient (or family member or lay-care giver) need to make informed decisions about their care (or care of the patient)?
- Will a patient (or family member or lay care giver) be reasonably expected to use the device?
- What written and audio-visual directions for use should be available to supplement directions given by the health care provider to assure safe and effective use of the device?
- What guidance must be given to patients to assist them in recognizing symptoms, problems or complaints associated with the use of the device that, if ignored, could lead to an adverse event.

Consult expert sources, (e.g., health care professionals, typical patients, literature, clinical studies) to ensure that you have considered all pertinent needs.

After considering these needs, the applicant should consider providing patient information labeling for devices that meet any of the following criteria:

1. Although the patient (or family member or lay care giver) may not directly select or use the device,
    - he or she must cooperate in the use of the device or supply important medical history information that may affect the safe and effective use of the device (e.g., ultrasound, MRI), or
    - the outcome of device use may be sensitive or affect others besides the patient (e.g., HIV test, genetic screening), or
    - device use extends beyond the immediate physician/patient interaction (e.g., implants not controlled by the patient that may be affected by an imaging procedure, or
2. The patient or lay care giver has some role in the actual selection or use of the device (e.g., OTC IVDs, home infusion pumps, implants controlled by the patient).

As with patient counseling information, the applicant often has the necessary information, from its clinical constituency, about what information is generally available and used to inform

patients about procedures and the devices used in them. The applicant may seek such information from various sources, such as their own or published animal studies or clinical studies, IRB deliberations, standard practices of care, insurers, professional organizations, advocacy groups, voluntary standards organizations, and governmental bodies, such as regulatory groups and CDC. Applicants need to consider this information in the proper context of user, environment where the device will be used, cultural and societal norms, and anthropometric data. It will be incumbent on the applicant to judge tradeoffs between informing patients properly of the important issues and burdening them with extraneous information.

Whether or not an applicant decides to provide patient information labeling for a device, the applicant should provide in the submission the rationale for this decision and any accompanying information that supports this rationale. It may be that a device does not meet the above criteria or that there is excellent patient information that has been developed and disseminated by a third party for which the applicant's effort would be needlessly duplicative. It will be important for the agency to know that patient information labeling has been considered and that a deliberate decision has been made concerning it.

When patient information labeling is provided, it shall include the indications, contraindications, warnings, precautions and adverse event or adverse reactions using terminology well known and understood by the target audience. Technical terms should be avoided, but when used, should be defined.

Written text should use short, simple sentences, using the active voice and few polysyllabic words. Type size should be chosen based on the needs of the target audience. Graphics should be used whenever appropriate to assist the reader to understand the text. Written patient information labeling should not generally exceed the seventh grade reading comprehension level.

Information for the patient should be tested on a sample of the expected target audience (i.e., focus group testing) to assure that it is understandable. For devices where a patient or family member or lay care giver is expected to operate the device, usability testing should a part of the device development to assure that the device and its operating instructions can be used and to identify potential problems or areas of misuse that may require special warnings or precautions to be placed in the labeling.

14. REFERENCES

Reference to primary (generally available) articles from refereed journals are not generally used as a source of clinical data. When appropriate, for example, citations to an established methodology description, please give complete citations in the National Library of Medicine (NLM) format (see GUIDANCE BIBLIOGRAPHY for examples). Use standard NLM abbreviations for the journal title.

*FDA review team **must** review all literature cited for appropriateness as is done for other labeling material. Particular care should be taken to assure that the articles do not contain unsupported claims or promotions.*

Glossary

Accompanying the Device Any materials that have been distributed by the manufacturer, distributor, supplier or other person responsible for the labeling of the product, whether the material is shipped with, precedes or follows the device's introduction into interstate commerce. This may include materials not traditionally sent with the device, including pamphlets, brochures, dear Dr. Letters, and reprints of journal articles.

Adopted Standards are those which the FDA finds useful in facilitating the review of medical devices. The 1995 FR notice ... describes such standards.

Adverse Events An undesirable effect reasonably associated with the use of a device.

Boxed Warning A warning that is highlighted by surrounding it with a border or box and placing it first in the format to demonstrate the very serious nature of that warning. For purposes of labeling a medical device, there is no further implication to this type of warning presentation, such as the advertising restriction associated with a boxed warning for a pharmaceutical product.

Contraindications Alerts the user to situations where the device should not be used because the risk of using the device always outweighs the benefit.

Directions for Use Information necessary to assist the user to operate the device safely and effectively. Such directions may need to be accompanied by diagnostic information, additional training, counseling by a health care professional or other information to ensure safe and effective use of the device. All devices, other than those exempted by 801.116, must have directions for use.

Essential Prescribing Information (EPI) Brief highlights of the important information contained in the full labeling that are necessary for the health care practitioner to determine whether a device is appropriate for a particular patient. The EPI should be no longer than one page and laid out according to the standard format (at the beginning of this guidance). The EPI is intended to provide an overview and refresher for those already familiar with the full labeling for the device and should be cross referenced to the full labeling.

Health Care Practitioner (or licensed practitioner?) An individual licensed by the law of the state in which he or she practices to use or order the use of a device.

Indications for Use An indication for use is "a general description of the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended."

Intended Use The objective intent of the persons legally responsible for the labeling of devices. The intent is determined by such persons expressions or may be shown by the circumstances surrounding the distribution of the article. This objective intent may, for example, be shown by labeling claims, advertising matter, or oral or written statements by such persons or their representatives.

Individualization of Treatment Information concerning specific characteristics of a device and/or of the patient that is necessary for the health care practitioner to determine if the device is appropriate for a specific patient. Such information may include physical limitations on the use of the device, administration guidelines, features and functions for specific populations (as supported in the

premarket submission). This information does not change the indications for use but rather assists the health care practitioner to properly match device and patient.

Label Any written, printed, or other communication medium upon the immediate container of any article. [Section 201(k) FD&C Act]

Labeling All labels and any other written, printed, or communication media upon any article or any of its containers or wrappers, or accompanying such article

Lay User A device user other than a licensed and trained health care practitioner. Such users may be patients, family members, friends, volunteers or hired care givers. They differ in education, literacy, primary language and life experience from professional users of medical devices.

Medical Device An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component part or accessory, which is

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease in man or other animals, or
- intended to affect the structure or any function of the body of man or other animals, and
- which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent on being metabolized for the achievement of its primary intended purposes.

Medical Device Reporting (MDR) The manufacturer of a medical device must report all postmarketing serious adverse events to the agency. The Safe Medical Devices Act of 1990 and the tentative final rule published in 1991 require medical device destributors and user facilities to report serious device related harm (serious injury or death) to the FDA and to the manufacturer (if known).

OTC Device A device for which the manufacturer can develop directions for use that a lay user can understand and follow to operate the device safely and effectively without health care practitioner supervision.

Precautions alert the reader to exercise special care necessary for the safe and effective use of the device. They may include actions to be taken to avoid effects on patients or users that may not be potentially life threatening or result in serious injury, but about which the user should be aware. Precautions may also alert the user to adverse effects on the **device** of use or misuse and the care necessary to avoid such effects.

Prescription Device A device which, because of any potentiality for harmful effect, or the method of its use, or the collateral measures necessary for its use is not safe except under the supervision of a health care practitioner.

Serious Refers to an adverse experience that is life threatening, results in permanent impairment of a body function or permanent damage to body structure, or necessitates medical or surgical intervention to preclude permanent of a body function or permanent damage to a body structure. (21 CFR 803.3)

Symbols A configuration consisting of an image with or without a surround shape, which conveys a message without the use of words. [ANSI Z535.3-1991]

Warnings alert the user to potential serious outcomes as in situations. Warnings focus on the potential for serious harm to the patient or user.

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END of DRAFT Guidance Document

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